ISO 9002-94 CERTIFIED
QUALITY MANAGEMENT SYSTEM

CYANOTECH CORPORATION

97 26 '00 AUG -8 P2:28

Thursday, July 06, 2000

RECEIVED
JUL 12 2000

Office of Special Nutritionals (HFS-450)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
200 C Street SW
Washington, DC
20204

RE: Notification of structure function statement of nutritional support (BioAstin)

Dear Administrator,

This letter in triplicate is notification of structure function statement of nutritional support for the dietary supplement, BioAstin per 21 CFR section 101.93.

Description of Product:

The trade name of the product is BioAstin, and consists of a spray-dried powder of *Haematococcus pluvialis* algae. The primary ingredient of the product is the carotenoid, astaxanthin. The microalgae is classified as follows:

Phylum:	Chlorophyta
Class:	Chlorophyceae
Order:	Volvocales
Family:	Haematococcaceae
Genus:	Haematococcus
Species:	pluvialis

Under GMP conditions, *Haematococcus* algae is formulated into an oil such as safflower and then packaged into gelcaps. The oil helps to enhance the bioavailability and stability of the carotenoids. The algae is also processed by standard commercial methods such as supercritical fluid extraction to obtain a concentrated oil extract. The concentrated oil can then be manufactured into water-dispensable or tablet-grade beadlets.

Astaxanthin, has had a long history of safe use in the human diet from salmon, shrimp, lobster and other seafood. Marketing clearance as prescribed by 21 CFR Subpart B 190.6 (New Dietary Ingredient Notification for *Haematococcus* algae) was completed August 6, 1999.

97S-0162

Let 5680

73-4460 Queen Kaahumanu Highway, #102 • Kailua-Kona, Hawaii 96740 • Phone (808) 326-1353 • Fax: (808) 329-3597

Statement of Nutritional Support:

The statement: "Free radical defense" is used for labels of BioAstin. The company has reviewed the scientific evidence supporting the statement of nutritional support and has concluded that it is truthful, scientifically valid, and not misleading. A symbol is linked to the disclaimer, "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease".

The statement "Helps combat free radicals" is used on another manufacturers product (Cell Tech- Super Sprouts and Algae).

Ingredients:

BioAstin is formulated to contain 2 milligrams of astaxanthin per gelcap from *Haematococcus pluvialis* algae. Foodgrade safflower oil is used as the carrier for the product.

Brief Scientific Summary:

Astaxanthin is a member of the carotenoid family, and elicits the pink to red hue of salmon, trout, lobster, crayfish, shrimp, seabream and many other seafoods. Numerous published papers have demonstrated the potent antioxidant capability of numerous carotenoids including astaxanthin.

Carotenoids, and especially astaxanthin, protect cells against oxidation by 1) quenching singlet oxygen and dissipating the energy as heat and 2) scavenging free radicals to prevent and terminate chain reactions. Due to its particular molecular structure, astaxanthin serves as an extremely powerful antioxidant. It has a very effective quenching effect against singlet oxygen, a powerful scavenging ability for lipid and free radicals and effectively breaks peroxide chain reactions (Kurashige et al. 1990; Jorgensen, 1993; Miki, 1991, Di Mascio, 1989, Terao, 1989).

Researchers have developed a variety of methods to measure the antioxidant capacity of carotenoids. Some of these assays are conducted in test tubes (in vitro) to better control conditions or within cells themselves (in vivo). Typically, a chemical that generates free radicals or peroxides is mixed with a substrate such as a fatty acid that can become readily oxidized. When the reaction rate is determined, carotenoids or other antioxidants can then be added to determine how it quenches, or slows the peroxidation rate of the fatty acid. Numerous studies exist demonstrating the potent radical scavenging and singlet oxygen quenching properties of astaxanthin (Haila, 1997;Woodall, 1997;Nakagawa, 1997;Oshima, 1993; Tinkler, 1994). It has been demonstrated that astaxanthin is significantly more effective in neutralizing free radicals than beta-carotene and protects against peroxidation of unsaturated fatty acid methyl esters better than canthaxanthin, beta-carotene or zeaxanthin (Terao, 1989; Jorgensen, 1993). In fact, the antioxidant activities of astaxanthin have been shown to be approximately 10 times

stronger than other carotenoids such as zeaxanthin, lutein, canthaxanthin and beta-carotene (Miki, 1991).

Di Mascio utilized a chemiluminescent technique to express the superior singlet oxygen quenching ability of astaxanthin compared to other carotenoids. He also concluded that the effectiveness and potency of astaxanthin was even better expressed at the lower oxygen concentrations found in tissues, as opposed to higher oxygen concentrations normally used with in vitro conditions (Di Mascio, 1989).

Although researchers use different assay systems, astaxanthin has been shown to surpass the antioxidant activity of other carotenoids such as zeaxanthin, lutein, beta-carotene and canthaxanthin. Astaxanthin has an activity over 500 times greater than alpha-tocopherol, also known as vitamin E (Di Mascio, 1989; Ranby and Rabek 1978; Shimidzu, 1996; Naguib, 2000). Vitamin E (tocopherol) is another key lipid-soluble antioxidant for the body. Interestingly, in vitamin E-deficient rats, astaxanthin can help restore the shortcoming and protect against damage caused by lipid peroxidation (Miki, 1991; Kurashige, 1990). One researcher has proposed astaxanthin as the "super vitamin E" (Miki, 1991).

In cell culture studies, similar results demonstrate the efficacy of astaxanthin as an antioxidant against peroxyl radicals. It was shown astaxanthin was more effective than beta-carotene, zeaxanthin or canthaxanthin in protecting membrane phospholipids from peroxidation (Lim, 1992).

In another report, primary cultures of chicken embryo fibroblasts (CEF) were oxidatively stressed by exposure to the herbicide, paraquat, as the radical generator while various levels of astaxanthin were added to ascertain the antioxidant effect. Activities of the antioxidant enzymes superoxide dismutase (SOD), catalase and glutathione peroxidase were measured as indices of oxidative stress. Without astaxanthin, paraquat increased the activities of SOD and catalase more than two-fold, and decreased the activity of glutathione peroxidase by more than 50% indicating high oxidative stress. Protection against paraquat-induced oxidative stress was observed at all levels of astaxanthin tested and was significantly greater than beta-carotene or vitamin E in this model (Lawlor and O'Brien, N.M., 1994). Other studies show that astaxanthin furnishes more protection to rat liver microsomes undergoing radical-initiated lipid peroxidation than either beta-carotene or vitamin E (Palozza, 1992; Nishigaki, 1994).

Clinical studies sponsored by the company are underway to further substantiate the antioxidant benefits of astaxanthin.

Intended Use:

The recommended daily dosage of BioAstin is 1 gelcap which provides 2 milligrams of astaxanthin. The product does not present a significant or unreasonable risk of illness or injury under the conditions of use suggested in the labeling. There are no known contraindications or warnings that need to be stated.

CYANOTECH CORPORATION

Manufacturer:
Cyanotech Corporation
73-4460 Queen Kaahumanu Highway #102
Kailua-Kona, HI
96740
Tel: 808-326-1353
Fax: 808-329-3597

The firm believes it has substantiation that the statements "Free radical defense" is appropriate, truthful and not misleading for the ingredients of BioAstin. If you have any questions or concerns, please do not hesitate to contact me.

Kind regards,

R. Todd Lorenz, Ph.D.
Scientific Director